UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/630,345	07/31/2000	Anand C. Burman	U 012858-1	5580

140 7590 04/23/2002

LADAS & PARRY
26 WEST 61ST STREET
NEW YORK, NY 10023

EXAMINER	
MOHAMED, ABDEL A	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 04/23/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/630,345	Applicant(s) BURMAN ET AL.	
	Examiner Abdel A. Mohamed	Art Unit 1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 January 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *10-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2,4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

ACKNOWLEDGMENT FOR IDS, RESPONSE TO SUPPLEMENTAL RESTRICTION REQUIREMENT AND STATUS OF THE CLAIMS

1. The information disclosure statement (IDS) and Form PTO-1449 filed 7/31/00 and 9/4/01, and the response to the supplemental restriction requirement filed 1/31/02, respectively are acknowledged, entered and considered. Claims 1-13 are now pending in the application.

ELECTION WITHOUT TRAVERSE

2. Applicant's election of Group I, claims 1-9 in Paper No. 9 is acknowledged. Although, Applicant has elected to prosecute the invention of Group I (claims 1-9) with traverse; however, since Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, and since there was no argument presented with the response to the election, except for the mere recitation that Applicant traverse this requirement. Hence, the election has been treated as an election without traverse (MPEP § 818.03(a)). Thus, it is advisable to cancel non-elected claims properly with an amendment stating "cancel claims 10-13" when responding to this Office action. Therefore, the Office action is directed to the merits of claims 1-9 (Group I) as per elected invention.

OBJECTIONS TO TRADEMARKS AND THEIR USE

3. The use of trademarks "LichroCART® C_{18}" and "C 18 Lichrospher® WP-300" have been noted in this application. The trademarks have not been capitalized, they should be capitalized whenever they appear and be accompanied by the generic terminology. Although, the use of trademarks are permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in a manner which might adversely affect their validity as trademarks.

Further, the specification which specifies the generic terminology should include published product information sufficient to show that the generic terminology or the generic description are inherent in the article referred by the trademarks. These description requirement are made because the nature and composition of articles denoted by trademark can change and affect the adequacy of the disclosure.

CLAIMS REJECTION-35 U.S.C. 112 1st PARAGRAPH.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the synthesis/preparation of peptide composition comprising a peptide of the general formula as recited in claim 1 and peptides of SEQ ID NOS:2-6 and using the above

peptides at different concentrations individually *in vitro* to determine the cytotoxicity effect or activity of the peptides in various human cell lines and *in vivo* antitumor activity on PTC tumor xenograft in nude mice, does not reasonably provide enablement for a therapeutically effective pharmaceutical composition containing individual peptides for treatment of cancer in mammals including humans by administering an effective mount of peptides of claims 1 thereof as recited in claim 9. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims; e.g., claim 9 is directed to "*in vivo*" "treatment" of any kind of cancer by administering "an effective amount" of the peptide of claim 1 as presently claimed without qualifiers, claim is directed to a pharmaceutical composition comprising an effective amount of a polypeptide; and as to the rest of the claims, they are directed to pharmaceutical compositions comprising the peptide composition claimed in claim 1 and the various sequences of claims 3-7 (i.e., SEQ ID NOS:2-6).

The instant specification on pages 3-8 teaches how to prepare and/or synthesize peptides of SEQ ID NOS:2-6 as disclosed in Examples 1-5. Example 6 shows the study of the cytotoxic effect of Lipo-peptide analogs of DT-A1, DT-B1, DT-01, DT-M, and DT-P1 (respectively, SEQ ID NOS:2-6) by MTT assay. Also, See the Tables disclosed on pages 9-11. Example 7 demonstrates the *in vivo* activity of Lipo-peptide analogs of DT-B1 (SEQ ID NO:3) in human colon adenocarcinoma (PTC) xenograft in nude mice. However, except for synthesis of the polypeptide claimed which is disclosed in Examples 1-5 and Example 6 which shows the

biological activities of the peptides *in vitro* by using cytotoxicity activity of the synthesized peptide analogs and various Tables and/or charts disclosing the percentages of cytotoxicity at different concentrations in various human tumor cell lines. Example 7 also demonstrates *in vivo* antitumor activity of substance P analogs on PTC tumor xenograft in nude mice which shows tumor volumes between treated and controlled groups. The above disclosure and the mere recitation on page 4, lines 15-17 in the instant specification by stating that the novel compounds of the present invention have important pharmacological applications. They are anti-neoplastic agents and thereby possess therapeutic potential in a number of human cancers would not entitle Applicant to a method of treatment of cancer in mammal in general by administering an effective amount of the polypeptide claimed because the scope of the instantly claimed invention are very broad and speculative in that there is no working example or data or evidence which shows that the claimed peptides individually are useful as a pharmaceutical composition by administering as an active ingredient a therapeutically effective amount of the peptide to treat cancer in mammals including humans in the manner claimed in the instant invention. There is no evidence in the instant specification to use or administer the pharmaceutical formulation in therapeutically effective composition as claimed. There is no dosage amount for pharmaceutical composition disclosed, except for the various *in vitro* assays which show the cytotoxicity effect or activity in human tumor cell lines with different concentrations of peptides and analogs as disclosed in Examples 1-7 and the various Tables and/or charts showing cytotoxicity percentages in the instant specification.

Thus, there are no sufficient data or evidence to substantiate such protocols of using a therapeutically effective pharmaceutical composition for treating cancer in general in the manner claimed. Hence, the only support for the claimed therapeutically effective pharmaceutical composition and method of treatment of cancer in mammals by administering a therapeutically effective dose of the pharmaceutical composition thereof in the specification is Applicant's supposition of the invention as recited in the protocols. Furthermore, Applicant's claims are directed to a very large number of compounds by using specific therapeutically effective amount of pharmaceutical composition, and there are no objective factual evidence in the specification showing that treatment has occurred using the specific therapeutically effective amount of pharmaceutical composition claimed. Thus, it is the Examiner's position that one can not administer specific effective amount of a pharmaceutical composition in all situations without appropriate testing which would require the exercise of undue experimentation, as for example, treating cancer in general in mammals.

Therefore, in view of the above, it would include those that have not been shown or taught to be useful or enabled by the disclosed method of making and using the invention. Moreover, undue experimentation is necessary to determine if and under what conditions, the claimed invention as broadly claimed is enabled, since a vast range of pharmaceutical composition in all kinds of possible compounds are contemplated and are encompassed as well as wide range of situations. The results desired appear to be highly dependent on all variables, the relationship of which are not present in the specification. Hence, one of ordinary skill in the art would not be

able to identify all the pharmaceutical preparations with the various peptides either alone or in combination having all kinds of concentrations intended to be effective for the claimed purpose as encompassed in the claims would be effective and under what conditions.

Further, the first paragraph of 35 U.S.C. 112 requires, inter alia, that a patent specification provide sufficient guidance to enable a person skilled in the art to make and use the claimed invention without undue experimentation. In re Vaeck, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991). While patent Applicants are not directed to disclose every species that falls within a generic claim, id. At 496, 20 USPQ2d at 1445, it is well settled that "the scope of the claims must bear a reasonable correlation to the scope of the enablement provided by the specification". In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Where practice of the full scope of the claims would require experimentation; factors to be considered in determining whether a disclosure would require undue experimentation ..... include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. In re Wands, 858 F. 2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Therefore, applying the Wands factors to the facts of this case, one of skill in the art would find that undue amount of experimentation would be required to practice the full scope of the extremely broad claims fro the reasons given above. Thus, in view of the quantity of experimentation necessary, the lack of adequate guidance or working examples or data. and the

breadth of the claims, the claims are not commensurate in scope with the enabling disclosure. Accordingly, filing of evidence commensurate with the scope of the claims or amendment of the claims to what is supported by the enabling disclosure is suggested.

CLAIMS REJECTION-35 U.S.C. § 112 2nd PARAGRAPH

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Independent claim 1 is indefinite in failing to recite as to the function or activity or use of the peptide of the formula referred in claim 1 (i.e., it is not clear what the peptide recited in claim 1 is supposed to do). Also, claim 1 is indefinite because the claim discloses sequences without the use of sequence identifier (See Sequence Rule 1.821(d)) which requires the use of SEQ ID NO even if the sequences is embedded in the text of the description or in the claim. Accordingly, all sequences must be referred to by use of an identifier such as "SEQ ID NO" which refers to the sequences as presented in the Sequence Listing, even though the sequence, itself may be embedded I the text of the application.

Claim 2 is indefinite in the recitation the selection of various alkanoyl groups because it is not clear if Applicant intends a Markush format. If Applicant intends to use a Markush format, then, the Office recommends the use of the phrase ".....selected from the group consisting of...." in listing species to ensure the Markush group is "closed".

Claim 7 is indefinite as to the "]" at the end of line of the claim as there is no corresponding "[". Appropriate correction is required.

Claim 9 is indefinite in the recitation "....administration of an effective amount...." because it is not clear what is meant by the terms "effective amount" since no amount of peptide is claimed or disclosed, and as such, the metes and bounds of the claims cannot be determined.

CONCLUSION AND FUTURE CORRESPONDENCE

6. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (703) 308-3966. The examiner can normally be reached on Monday through Friday from 5:30 a.m. to 5:00 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (703) 308-2923. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

AMohamed/AAM

April 19, 2002